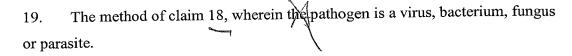
## WHAT IS CLAIMED IS:

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- 1. A high-throughput method of screening compounds capable of modulating topoisomerase activity comprising:
- (a) incubating at least a first nucleic acid, a topoisomerase and a potential topoisomerase-modulating compound, wherein the nucleic acid comprises at least one tag, and
- (b) assaying for nucleic acid religation.
- 2. The method of claim 1, wherein the nucleic acid is DNA.
- 3. The method of claim 1, wherein the nucleic acid is RNA.
- 4. The method of claim 1, wherein the at least one tag is a detection tag or an affinity tag.
- 5. The method of claim 1, wherein the method comprises incubating at least a first nucleic acid and a second nucleic acid.
- 6. The method of claim 5, wherein the second nucleic acid is a religation strand comprising oligonucleotides operatively associated with at least one marker tag.
- 7. The method of claim 6, wherein the first nucleic acid is operatively associated with an affinity tag and the second nucleic acid is operatively associated with a detection tag.
- 8. The method of claim 1, wherein the assay detects for topoisomerase inhibitors

- 9. The method of claim 1, wherein the assay detects for topoisomerase activators.
- 10. The method of claim 1, wherein the topoisomerase is a Type I or Type III topoisomerase.
- 11. The method of claim 1, wherein the topoisomerase is a Type II or Type IV topoisomerase.
- 12. The method of claim 1, wherein assaying comprises measuring the level of nucleic acid religation activity in the presence and absence of the topoisomerase-modulating compound
- 13. The method of claim 1, wherein the level of religation activity is inversely proportional to the effectiveness of the topoisomerase-inhibitory compound.
- 14. The method of claim 1, wherein step (a) is performed on a solid support.
- 15. The method of claim 1, wherein step (a) is performed in a liquid phase.
- 16. The method of claim 1, wherein the nucleic acid and topoisomerase are covalently complexed, wherein the topoisomerase retains its religation activity.
- 17. A method of treating cancer comprising administering a pharmaceutical composition comprising a topoisomerase inhibitor to a patient in need thereof.
- 18. A method of treating an infection by a pathogen comprising administering a pharmaceutical composition comprising a topoisomerase inhibitor to a patient in need thereof.



- 20. A kit for screening compounds that modulate topoisomerase religation activity comprising:
- (a) a substrate nucleic acid comprising a first tag,
- (b) a religation nucleic acid comprising a second tag,
- (c) a topoisomerase, and
- (d) a means for measuring nucleic acid religation activity of a test mixture comprising (a). (b) and (c) in the presence or absence of a topoisomerase-modulating compound.
- 21. A high-throughput method of screening compounds capable of modulating nucleic acid-modifying enzymatic activity comprising:
- (a) incubating at least a first nucleic acid, a nucleic acid-modifying enzyme and a potential enzyme-modulating compound, wherein the nucleic acid comprises at least one tag, and
- (b) assaying for nucleic acid religation or cleavage.

